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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,947	KADOUCHE ET AL.	
	Examiner	Art Unit	
	David A. Saunders	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 18-48* is/are pending in the application.

4a) Of the above claim(s) *8-9,32-35,37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10-16,18-31,36 and 38-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS PENDING

Claims 1-16 and 18-48 are pending.

Applicant's election without traverse of Species II (claims 38-40 and 44-48) in the reply filed on 4/28/08 is acknowledged.

Claims 1-7, 10-16, 18-31, 36 and 38-48 are under examination.

OBJECTION(S) TO DISCLOSURE

The disclosure is objected to because of the following informalities:

The spacing of the lines of the specification is such as to make reading difficult. New application papers with lines 1½ or double spaced on good quality paper are required.

Because of the above noted informality, throughout this action the examiner will refer to portions of applicant's disclosure by reference to paragraph numbers in square brackets, as they appear in the US Pre-Grant Publication of this application. This publication is cited on attached Form PTO-892.

OBJECTION(S) TO CLAIMS

Claim(s) 3-4 is/are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 3-4 do not further limit base claims 1-2 for the following reasons:

Base claim I refers to a "compound of interest", and claim 2 then states that this "compound of interest" is an "antigen". In claim 3, however, numerous of the recited "antigens" constitute far more than a single "compound". For example, "viral particles" are made up of many macromolecular "compounds". The "organs, organelles, whole cells and subcellular fragmentations" are even more complex than any viral particle. Likewise, the tumor cells of claim 4 are even more complex than any viral particle

Claim(s) 20 is/are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 20 further defines step (16) of claim 1 by requiring the "selection of at least one cell secreting a monoclonal antibody with specificity and/or affinity for said compound". On the other hand, step (16) of claim 1 only requires the selection of at least one cell secreting an "antibody with affinity for said compound". Thus if one conducts claim 20 according to the embodiment in which one conducts the "selection of at least one cell secreting a monoclonal antibody with specificity…for said compound", one is conducting a method that is not within the scope of step (16) of claim 1.

Claim 20 also does not further limit step (16) of base claim 1 since it is not clear what would the criterion of "selection" in step (16) of claim 1, other than that the "at least one cell" would be selected on the basis that it exhibits a secretion of a "specific monoclonal antibody with affinity for said compound" to a degree "greater than… other cells".

REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claims 1-7, 10-16, 18-31, 36 and 38-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "large-scale" in claim 1, line 1 thereof, is a relative term which renders the claim indefinite. The term "large-scale" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The term "automated" in claim 1 is indefinite because applicant's own definition of the word "automated" (para. [0025]) has indicated that this word "should be understood to mean that all essential steps of the method, in accordance with the invention may be, and are preferably automated." One therefore has no idea what the

meets and bounds of the invention may be in terms of which of the steps of claim 1 or of any dependent claim are "automated". Even if applicant's definition had stated that this word "should be understood to mean that all essential steps of the method in accordance with the invention are automated", the claims would remain indefinite because applicant has failed to define what the "essential steps" actually are. Are all steps recited in the claims the "essential steps"? As noted, in 112, first para. rejections infra, there are at least some steps recited in the claims which cannot be automated; thus one has no idea what would be meant, even if applicant were to limit the claims such that "all essential steps" of the method were to be "automated".

Claim 1 is confusing since lines 2-3 refer to a "specific monoclonal antibody with affinity for a compound", while line 12 refers to an "antibody interacting with a compound". The claim has set forth no clear nexus between specificity for and interaction with a compound. This confusion follows through to numerous dependent claims – e.g. claim 16 which recites "interacting".

In claim 7, it is unclear what the "antibody-producing cells" are recovered from.

The term "concomitant" in claims 30 and 47, is a relative term which renders the claim indefinite. The term "concomitant" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Since the examiner has indicated further infra, under 112, first paragraph issues, that there is no way that the measurement of affinity and the identification of or location of at least one epitope of said compound has been shown to be conducted with the use of a single apparatus, one is unsure of what the term "concomitant" means. If the measurement of affinity and the identification of or location of at least one epitope of said compound cannot be conducted with the use of a single apparatus, then there must be something sequential in the manner in which these steps are conducted; how then can they be considered "concomitant"?

REJECTION(S) UNDER 35 USC 112, FIRST PARAGRAPH

Claims 1-7, 10-16, 18-31, 36 and 38-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant was not in possession of the invention for the case in which all of the claimed steps are automated; in such case, applicant has not shown the structural cooperative relationships of the elements of an apparatus which would conduct all of the steps. Applicant appears to have contemplated the use of art standard ELISA screening machines (e.g. para. [0076]), automated evaluation of antibody affinity with an art standard Biacore instrument (para. [0126]), automated distribution of hybridoma cells into wells (e.g. para [0235]), automated cloning of positive hybridoma cells (e.g. para. [0256]) and automated reading of plates (e.g. para. [0265]); however, one finds nothing in the claims that shows what elements connect the various aspects of the overall method, so that all steps of the entire claimed process are automated -- e.g. what elements connect a dish with a ground up spleen (para. [0229]) to a primary screening module (para. [0248]+)? What elements connect a culturing apparatus to a screening apparatus? What elements connect the secondary screening module to a tertiary screening module -- e.g. what elements select the positive Mab secreting supernatants of the secondary screen to a Biacore apparatus (para. 0272]). What elements connect the tertiary screening module to a Western blot method (para. [0274])?

Furthermore, the term "automated" in claim 1 has been noted as being indefinite (see 112, 2nd rejection supra), because the word "automated" can be "understood to mean that all essential steps of the method, in accordance with the invention may be, and are preferably automated" (para. [0025]). One therefore has no idea what the specification should show, in terms of what elements must be provide to connect, for example, a culturing apparatus to a screening apparatus. Because applicant's own definition of the term "automated" has hedged on the issue of how much of the claimed

process is actually automated, and because applicant's disclosure is devoid of teachings that pertain to the structural cooperative relationships of the elements of an apparatus which would conduct all of the steps; applicant's disclosure can be taken as having described no more than conducting as many of the steps as one wishes, with already commercially available units, such as ELISA screening machine (para. [0076]).

Claims 30 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant has not disclosed an apparatus which is capable of automatically conducting step (15421), the measurement of affinity, and step (15422), the identification or location of at least one epitope of said compound, in a "concomitant" manner. Applicant has disclosed that, for example, the affinity of the antibodies is analyzed using a "Biacore 3000" type apparatus (paras. [0126] and [0272]). On the other hand, Applicant has disclosed that, for example, the mapping of epitopes is conducted with the use of a 2D electrophoretic system (para. [0132]). Since a "Biacore 3000" type apparatus and a 2D electrophoretic system are different apparatus systems and measure different features of the antibody being selected, there is no way that the measurement of affinity and the identification of or location of at least one epitope of said compound can be conducted in a "concomitant" manner.

Claims 7 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the case in which the "preliminary steps are not automated" (as in dependent claims 13 and 36, does not reasonably provide enablement for the case in which the "preliminary steps" are automated". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Specifically, the "immunization of at least one animal" [claim 7, step (1)] is not readily amenable to automation. Animals squirm and this tendency can be minimized by art known devices to restrain the movement animals during an immunization and/or a bleeding. However, none of the devices are "automated" in the sense that they can grab an animal, place it in the device and automatically inject antigen and/or draw a blood sample, without manual manipulation by a technician. Additionally, the "recovery of the antibody producing cells" [claim 7, step (3)], for example from a spleen, is not readily amenable to automation.

Applicant's disclosure has adequately indicated that steps such as the seizing, moving, or positioning of a culture, storing of a plate, collecting a liquid medium from a plate, washing of a well in a plate, (para. [0183]-[0187]) are amenable to automation by robotic means. Unlike animals, plates do not squirm. Unlike spleens, the position of a single well is fixed. Applicant is required to show on the record that an "automated" method for conducting all the steps of claims 7 and 10-12 was art known and available to the public at applicant's effective filing date, or else incorporate the limitations of claims 13 or 36 into claims 7 and 10-12.

REJECTION(S) UNDER 35 USC 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 7, 10-14, 16, 20, 26, 36, 41 and 43 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Schenk et al (6,287,793, cited on 892).

Schenk et al show screening for monoclonal antibodies against antigen(s) present in plasma from patients with Alzheimer's disease. See Example I. Steps corresponding to steps (1) and (3) of instant claim 7, as well as steps (4) and (5) of instant claim 10, are conducted conventionally (apparently manually); see col. 14, lines 19+. The "distribution" step (10) of instant claim 1 is apparently conducted manually. The "culturing" step (12) of instant claim 1 is apparently conducted manually. The "screening" step (14) of instant claim 1 is conducted by an automated screening of the supernatants of culture media; see col. 11, line 60-col 12, line 7. The "selecting" step (16) of instant claim 1 is shown at col. 12, lines 8-28; just how much of this was automated is unclear (e.g. does a "Screen Machine" of Pandex Labs conduct the statistical analysis of readings, as well as the recording of the fluorescence readings?); whether the selection of hybridomas secreting monoclonal antibodies (Mabs) 3H6, 5D8, 3H11 and 7-C1 was the result of an automated statistical selection method or a mental method need not be addressed in this rejection. All that is necessary for anticipation is that one of the steps of instant claim 1 be shown as "automated"; as noted supra, this one "automated" step is "screening" step (14). The reason that it is only necessary that one of the steps of instant claim 1 be shown as "automated" is that applicant's disclosure (see para. [0025]) has hedged on what is meant by the term "automated".

From the above, instant claims 1-3, 7, 10-13 and 36 are anticipated.

Regarding dependent claim 14, it is to be noted that culture medium (supernatant) is "transferred into at least one well of at least one screening plate" (see col. 11, lines 64-66). The "selection criterion" is the binding of the screened for Mabs to pooled Alzheimer's disease plasma (col. 12, lines 8-12). The "subculturing" of the cells is shown at col. 12, lines 20-24. The final "detection of cell growth" can either be

considered as being inherent or ,alternatively, as conventional in the art and hence obvious.

Regarding dependent claims 16 and 26, the above considerations pertaining to claim 14 likewise apply, if one considers that the binding of the screened for Mabs to pooled Alzheimer's disease plasma (col. 12, lines 8-12) constitutes as "primary screening", which it is, since Schenk et al conduct a "secondary" screening at col. 12, lines 10-19. (The Office has not rejected further dependent claim 18, because it does not appear that there was any "subculturing" conducted between the "primary" and the "secondary" screening steps of Schenk et al).

Claim 20 is rejected because the statistical selection criteria used by Schenk et al certainly constitute a method of selection such that the selected hybridoma cells secret Mabs having a specificity and or affinity for Alzheimer's disease plasma that is "greater than those of the monoclonal antibodies secreted by other cells."

Instant claims 41 and 43 are rejected because Schenk et al screened at "around day 10" (col. 12, lines 45-49).

Claims 1-7, 10-16, 18-31, 36 and 38-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harlow et al in view of Schenk et al, Salfeld et al, and Applicant's admitted state of the art.

Harlow et al show the art standard general scheme (p 149) for immunizing mice with an antigen, checking for any immune response, obtaining spleen cells from the mice, fusing the spleen cells with myeloma cells, culturing fused cells in multiple well arrays, screening the supernatant of each well for production of a monoclonal antibody (Mab) that binds a target antigen, subcloning, and further screening. Harlow et al disclose that there can be further rounds of screening that characterize a selected MAb for its specificity and/or affinity for antigen, or for its class/subclass (p 231). Salfeld et al are relied upon for teaching that it is known how to select Mabs according to their binding affinities and/or for their biological properties (e.g. neutralization of a biological activity of a target antigen). Salfeld et al are also relied upon for teaching that it is known

that Mabs could be obtained by a screening method that starts with a phage "library", instead of with spleen cells from an immunized mouse.

Thus Harlow et al and Salfeld et al teach that all of the steps of the instant method were known. The methods disclosed in the Harlow et al reference can be characterized as essentially "manual" – e.g. in terms of the transfer of culture fluids for culturing, subculturing, or for screening analysis. The claims are rejected on the basis that "broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result does not distinguish over the prior art." In re Venner, 120 USPQ 193. It is noted that instantly, the claims pertain to broadly providing an automatic means to replace a manual activity which accomplished the same result, and that the disclosure is devoid of any particulars as to how to do this, other than that one can use art-known automated machines for such tasks as: conducting an ELISA screening method (e.g. para. [0076]), a Biacore instrument which measures affinities and automatically conducts calculations (para. [0126], or admittedly art conventional robotic means for such tasks as "seizing, moving, positioning…storing…collecting liquid medium…washing….and data acquisition (para. [0182]-[0195]). In view of the fact that applicant's disclosure (see para. [0025]) has hedged on what is meant by the term "automated", all that is necessary for anticipation is that one of the steps of instant claim 1 be shown as "automated". As the Office has indicated supra in the 102/103 rejection over Schenk et al alone, this reference certainly shows automation of an ELISA screening method. Therefore, even if all other steps were to be manually conducted, claim 1 and all of its dependents would have been obvious.

Because applicant's own definition of the term "automated" has hedged on the issue of how much of the claimed process is actually automated, and because applicant's disclosure is devoid of teachings that pertain to the structural cooperative relationships of the elements of an apparatus which would conduct all of the steps; applicant's claims can be interpreted as encompassing no more than conducting as many of the steps as one wishes, with already commercially available units, such as ELISA screening machine (para. [0076]).

As to the automation of other steps, Salfeld et al indicated that a Biacore apparatus, for measuring affinities, can calculate on and off rates by software (col. 32, lines 40-44). This is consistent with applicant's considerations of what "automatic" means, as set forth at para. [0170]-[0172]. Further since robotic operations such as seizing, moving, positioning and storing objects, as well collecting and dispensing liquids, are art standard; automation of the steps pertaining to culturing, subculturing, etc. would have been obvious.

ART OF INTEREST

Art made of record and not relied upon is considered pertinent. Drake et al (US 2005/0260743, cited on 892) shows an automated method of cell selection and culturing. The US filing date post-dates the instant International filing date.

CONTACTS

Any inquiry concerning this communication from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 8/14/08 DAS

/David A Saunders/

Primary Examiner, Art Unit 1644